REMARKS

The Examiner asserts that claims 1-7, 10 and 11 fail to comply with the enablement requirement. Applicants respectfully cancel claims 2-6 in response to the Examiner's rejection, but submit that the Examiner's rejection on claims 1, 7, 10, and 11 is improper.

The Examiner states that the conclusion of instant invention is in contradiction to that of Selvaraju et al., which teaches inducing differentiation of oligodendrocyte precursor cells and enhancing remyelination by increasing exposure of oligodendrocyte precursor cells to OPN. The Examiner further states the following evidence to support his conclusion:

1) The cell lines, Oli-neu and CG-4, used in Selvaraju et al. are the oligodendrocyte precursors, and have been well-characterized and further demonstrated as being suitable for myelination study.
2) Selvaraju et al. did show proliferation, migration or differentiation of Oli-neu or CG-4 in response to OPN.
3) The conclusion from Selvaraju et al. is contradictory to that of instant invention.

Applicants respectfully amend Claim 1 to specify that oligodendrocytes are primary oligodendrocytes. The cell lines that Selvaraju et al. used are not primary oligodendrocyte cells and have different characteristics than primary oligodendrocyte cells. For example, cell lines, such as the CG4 cell line, are not representative of normal oligodendrocytes as the evidence has been shown in the same reference the Examiner gave for CG4 cell line as characterized as OLPs (Louis et at., 1992, J. Neurosci. Res., 31 :193-204). Louis et al. shows that CG4 can express GFAP and become astrocytes, which would never happen to normal oligodendrocyte progenitors. Moreover, much literature strongly supports the assertion of advantages to using real oligodendrocyte progenitor cells instead of cell lines. Cao et al. (1997, The Journal of Cell Biology, 138:1367–77) clearly states that "Oligodendrocyte precursor cells isolated from the developing rat optic nerve offer a number of advantages for studying the mechanisms that control cell proliferation and the timing of differentiation.... Fourth, unlike cell lines, they are normal cells and, with the addition of the appropriate signaling molecules, purified precursor

cells in serum-free clonal culture divide a limited number of times before they stop dividing and terminally differentiate into postmitotic oligodendrocytes, just as they do in vivo ..." (p1372-73)

In short, the CG4 cell line is not a normal primary oligodendrocyte and it has different characteristics from normal primary oligodendrocytes. The experiments on differentiation of primary oligodendrocytes are different than that of cell lines. Therefore, the conclusion from the experiments (models/assays) of instant invention is not surprisingly different from that of Selvaraju et al.

The examiner alleges that "Due to the large quantity of experimentation necessary to determine how to modulate differentiation of oligodendrocytes and enhance remyelination by reducing exposure of oligodendrocytes and precursors to OPN, or by first increasing exposure of oligodendrocyte precursor cells to OPN, then reducing the exposure to OPN, using unidentified molecules or antibodies, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that OPN stimulates differentiation and remyelination of oligodendrocytes, and the breadth of the claim which fails to recite particular activities and structure features for antagonists and antibodies etc., undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope" (Office Action, pages 5-6).

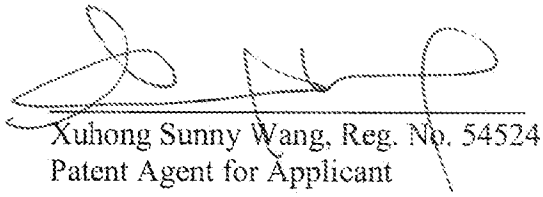
Applicants respectfully dispute this allegation. Claim 1 features, "A method of modulating differentiation of primary oligodendrocytes comprising reducing exposure of oligodendrocytes and precursors thereof to osteopontin" and claim 7 features "A method of modulating differentiation of primary oligodendrocytes, according to Claim 1, further comprising increasing exposure of oligodendrocyte precursor cells thereof at a remyelination site to osteopontin to enhance oligodendrocyte precursor number at said site, and then reducing exposure, according to Claim 1, of said oligodendrocyte precursor cells to osteopontin thereby enhancing differentiation into oligodendrocytes, wherein said oligodendrocytes enhance remyelination at said remyelination site". Because similar experiments have been carried out in much literature, including some that the Examiner has cited, the skilled artisan in the field

shouldn't have any difficulty making and/or using the claimed invention in its full scope. However, both the experiment and the result of the study on "modulating differentiation of primary oligodendrocytes comprising reducing exposure of oligodendrocytes and precursors thereof to osteopontin" are unique. That's what the instant invention claims.

In view of the above remarks, the Examiner's rejection is clearly improper and Applicants respectfully request that it be withdrawn. Early notice to this effect is, thus, respectfully requested.

The Commissioner is hereby authorized to charge the fee required and any additional fees that may be needed to Deposit Account No. 18-1982 in the name of sanofi-aventis U.S. LLC.

Respectfully submitted,



Xuhong Sunny Wang, Reg. No. 54524
Patent Agent for Applicant

sanofi-aventis U.S. LLC
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807
Telephone (908) 231-**3648**
Telefax (908) 231-2626

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